SCHEDULE 2

$$\textbf{Degree of Fluctuation} = \frac{C^{ss}{}_{\max} - C^{ss}{}_{\min}}{C^{ss}{}_{\min}} * 100\ \%$$

Where

$$C^{ss}{}_{\max} = \frac{FDose}{V_d}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-kt'_p}\ , \quad \text{with } t'_p = 2.303 * \log\frac{k_a(1-e^{-k\tau})/k(1-e^{-k_a\tau})}{k_a - k}$$

$$C^{ss}{}_{\min} = \frac{k_a FDose}{V_d(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}$$

F = Fraction Absorbed
k_a = Absorption Rate Constant
k = Elimination Rate Constant
V_d = Apparent Volume of Distribution
τ = Dosing Interval

By substituting the above $C^{ss}{}_{max}$ and $C^{ss}{}_{min}$ equations into the Degree of Fluctuation equation:

$$\textbf{Degree of Fluctuation} = \frac{\left(\frac{FDose}{V_d}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-kt'_p}\right) - \left(\frac{k_a FDose}{V_d(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}\right)}{\frac{k_a FDose}{V_d(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}} * 100\ \%$$

$$\rightarrow \quad \frac{\frac{FDose}{V_d}\left[\left(\frac{1}{1-e^{-k\tau}}\right)e^{-kt'_p} - \left(\frac{k_a}{(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}\right)\right]}{\frac{FDose}{V_d}\left(\frac{k_a}{(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}\right)} * 100\ \%$$

By canceling out the term $\frac{FDose}{V_d}$ $\rightarrow$

$$\frac{\left(\frac{1}{1-e^{-k\tau}}\right)e^{-kt'_p} - \left(\frac{k_a}{(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}\right)}{\frac{k_a}{(k_a-k)}\left(\frac{1}{1-e^{-k\tau}}\right)e^{-k\tau}} * 100\ \%$$

Rearranging the equation further → $$\frac{\frac{1}{1-e^{-k\tau}}\left(e^{-kt'_p} - \frac{k_a}{(k_a-k)}e^{-k\tau}\right)}{\frac{1}{1-e^{-k\tau}}\left(\frac{k_a}{(k_a-k)}e^{-k\tau}\right)} * 100\ \%$$

Finally, by cancelling out the term $\frac{1}{1-e^{-k\tau}}$ → $$\frac{\left(e^{-kt'_p} - \frac{k_a}{(k_a-k)}e^{-k\tau}\right)}{\left(\frac{k_a}{(k_a-k)}e^{-k\tau}\right)} * 100\ \%$$

$\therefore$ **Degree of Fluctuation** $$= \frac{\left(e^{-kt'_p} - \frac{k_a}{(k_a-k)}e^{-k\tau}\right)}{\left(\frac{k_a}{(k_a-k)}e^{-k\tau}\right)} * 100\ \%$$

CONCLUSION:

- **Degree of Fluctuation is dose independent**
- **Degree of Fluctuation is dependent on absorption and elimination rates and the dosing interval**